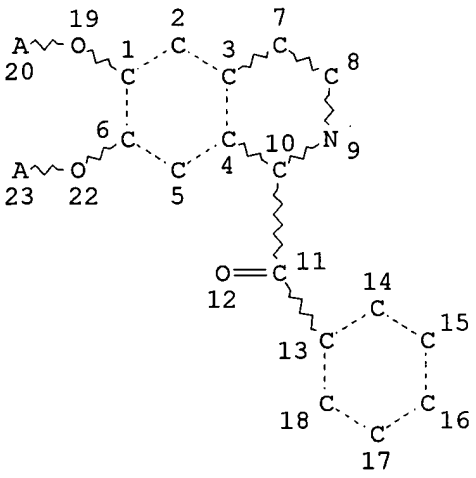
Northington-Davis
60/511954

(FILE 'REGISTRY' ENTERED AT 12:34:05 ON 28 OCT 2004)

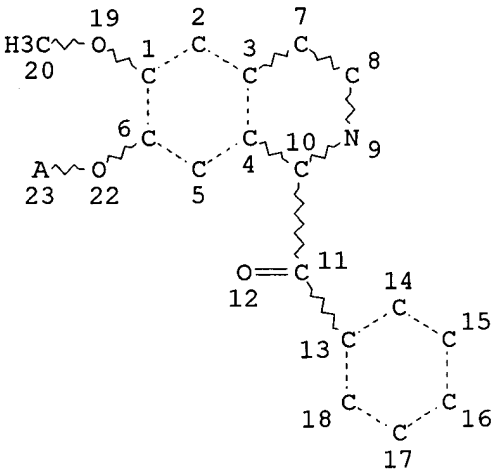
L1 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 20
NSPEC IS RC AT 23
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
L3 303 SEA FILE=REGISTRY SSS FUL L1
L8 STR



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DEFAULT MLEVEL IS ATOM
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Searcher : Shears 571-272-2528

GRAPH ATTRIBUTES:
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NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE
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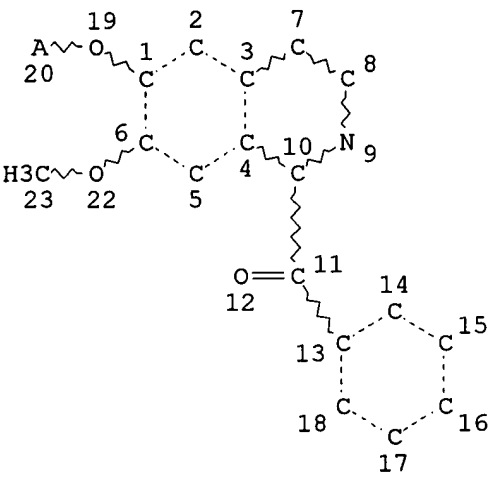


NODE ATTRIBUTES:
NSPEC IS RC AT 20
CONNECT IS M3 RC AT 7
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 22

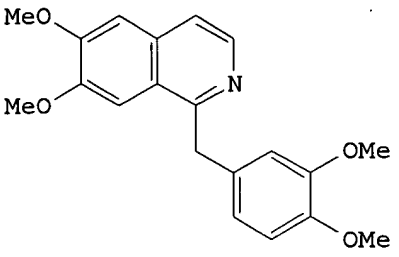
STEREO ATTRIBUTES: NONE
L10 2 SEA FILE=REGISTRY SUB=L3 SSS FUL (L8 OR L9)

100.0% PROCESSED 303 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FILE 'CAPLUS' ENTERED AT 12:36:09 ON 28 OCT 2004
L11 4 S L10

L11 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1989:595186 CAPLUS
DOCUMENT NUMBER: 111:195186
TITLE: Vanadic oxidation of papaverine in 2.5 M and 5 M sulfuric acid
AUTHOR(S): Postaire, E.; Martinez, D.; Viel, C.; Chastagnier, M.; Hamon, M.
CORPORATE SOURCE: Lab. Chim. Anal., Fac. Pharm., Chatenay-Malabry, 92290, Fr.
SOURCE: Bulletin de la Societe Chimique de France (1988), (6), 982-8
CODEN: BSCFAS; ISSN: 0037-8968

DOCUMENT TYPE: Journal
LANGUAGE: French
OTHER SOURCE(S): CASREACT 111:195186
GI



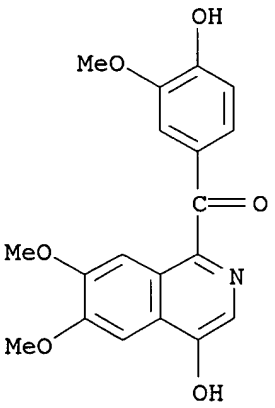
I

AB Vanadic oxidation of papaverine (I) in 5 M H2SO4 media shows a full oxidation
into carbon CO2 and water. However, according to the exptl. conditions, and in 2.5 M and 5 M H2SO4 media, intermediates and products have been identified: papaveraldine, hemipinimide, m-hemipinic acid, 6,7-dimethoxyisoquinoline, 1-formyl-6,7-dimethoxyisoquinoline, 1-acetyl-6,7-dimethoxyisoquinoline, 4-hydroxy-6-demethylpapaveraldine, 4-hydroxy-4'-demethylpapaveraldine, 3-hydroxy-6-demethylpapaveraldine and 3-hydroxy-4'-demethylpapaveraldine.

IT **115698-48-1P**
RL: FORM (Formation, nonpreparative); PREP (Preparation)
(formation of, in vanadic oxidation of papaverine)

RN 115698-48-1 CAPLUS

CN Methanone, (4-hydroxy-6,7-dimethoxy-1-isoquinolinyl)(4-hydroxy-3-methoxyphenyl)- (9CI) (CA INDEX NAME)



L11 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1988:473702 CAPLUS
DOCUMENT NUMBER: 109:73702
TITLE: Identification of the novel structures of

benzoyl-1-isoquinolines obtained by oxidation of papaverine

AUTHOR(S): Postaire, Eric; Viel, Claude; Martinez, Didier; Likforman, Joseph; Hamon, Michel

CORPORATE SOURCE: Fac. Sci. Pharm. Biol. Paris-Sud, Chatenay Malabry, 92290, Fr.

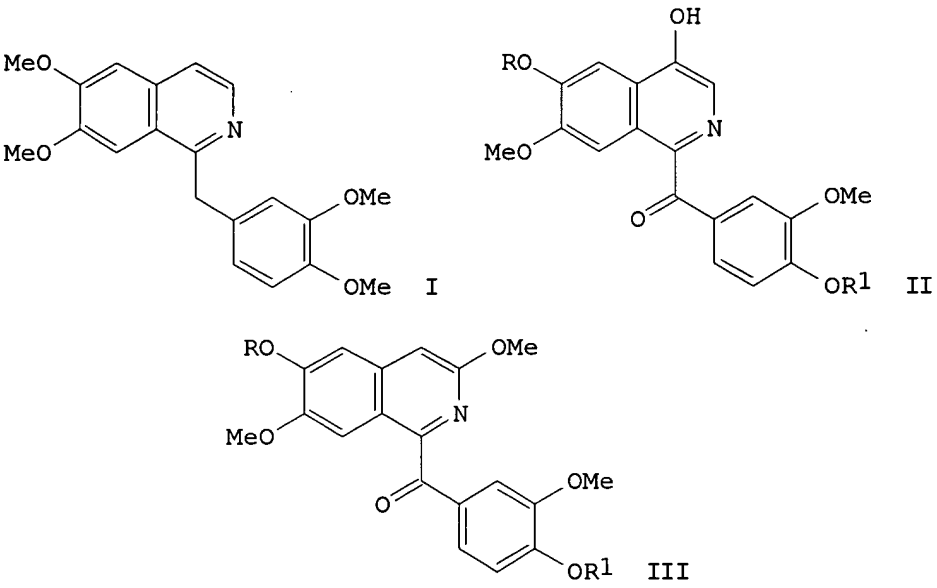
SOURCE: Chemical & Pharmaceutical Bulletin (1987), 35(10), 4064-7
CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: French

OTHER SOURCE(S): CASREACT 109:73702

GI

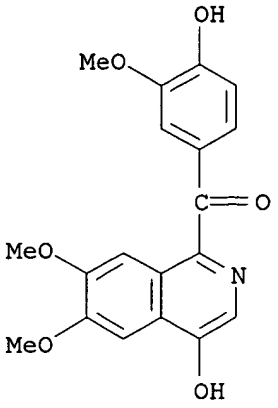


AB Papaverine (I) was oxidized by vanadium pentoxide in 2.5M aqueous H2SO4 to give 4 new compds.: 4-hydroxy-6-demethylpapaveraldine (II; R = H, R1 = Me), 4-hydroxy-4'-demethylpapaveraldine (II; R = Me, R1 = H), 3-hydroxy-6-demethylpapaveraldine (III; R = H, R1 = Me), and 3-hydroxy-4'-demethylpapaveraldine (III; R = Me, R1 = H).

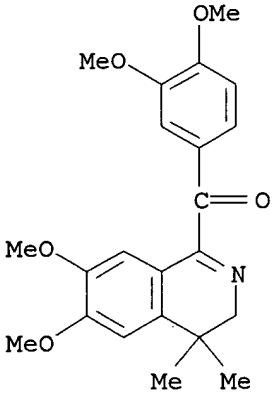
IT **115698-48-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 115698-48-1 CAPLUS

CN Methanone, (4-hydroxy-6,7-dimethoxy-1-isoquinolinyl)(4-hydroxy-3-methoxyphenyl)- (9CI) (CA INDEX NAME)



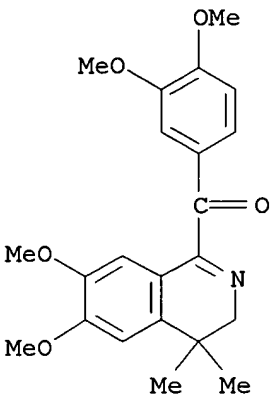
L11 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1964:440346 CAPLUS
DOCUMENT NUMBER: 61:40346
ORIGINAL REFERENCE NO.: 61:6988f-h,6989a-d
TITLE: Synthesis of 1-(4-methoxybenzoyl)-N-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline
AUTHOR(S): Wiegrebe, W.
CORPORATE SOURCE: Tech. Hochschule, Brunswick, Germany
SOURCE: Arch. Pharm. (1964), 297(6), 362-7
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The synthesis of the title compound (I) was described. Piperonal (10 g.), 10 g. MeNO2, 40 g. AcOH, and 4 g. NH4OAc refluxed 1 hr. gave 72% 3,4-methylenedioxy-ω-nitrostyrene (II), m. 158°. LiAlH4 reduction of II in tetrahydrofuran (THF)-ether gave 68% corresponding amine (III), b2 82°; III.HCl m. 214° (Me2CO). III (6 g.) treated with 8.3 g. p-MeOC6H4CH2COCl in C6H6 gave 71% N-[β-(3,4-methylenedioxyphenyl)ethyl] homoanisamide (IV), m. 98°. Cyclization of 5 g. IV was effected by refluxing it with 2.5 g. POCl3 in C6H6 1 hr. to give 4.4 g. (crude) V. On saturation with O in EtOH for 18 hrs., V gave 67% 1-anisoyl-5,7-methylenedioxy-3,4-dihydroisoquinoline (VI), m. 141° (EtOH). VI refluxed 5 hrs. with MeI (100% excess) in EtOH gave the quaternary salt (83%, m. 224°) which (1.5 g.) on reduction with 1 g. NaBH4 gave 69% corresponding carbinol (VII), m. 124° (MeOH). Oxidation of 0.5 g. VII with 1 g. tert-BuOK and 2 g. fluorenone in absolute C6H6 under N 18 hrs. gave 0.08 g. (crude) I, m. 132° (MeOH). I gave a pos. test with tetraphenyltetrazolium chloride. The ultraviolet spectra of VI, 3,4-dihydropapaveraldine (VIII), and the 4,4-Me2 derivative of VIII were recorded.
IT **95133-88-3**, Ketone, 3,4-dihydro-6,7-dimethoxy-4,4-dimethyl-1-isoquinolyl 3,4-dimethoxyphenyl
(spectrum of)
RN 95133-88-3 CAPLUS
CN Ketone, 3,4-dihydro-6,7-dimethoxy-4,4-dimethyl-1-isoquinolyl 3,4-dimethoxyphenyl (7CI) (CA INDEX NAME)



L11 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1962:456447 CAPLUS
DOCUMENT NUMBER: 57:56447
ORIGINAL REFERENCE NO.: 57:11251c-h
TITLE: Synthesis and hydrolytic degradation of DL-4,4-dimethyl-9-hydroxylaudanosine methiodide
AUTHOR(S): Wiegrebe, W.; Awe, W.
CORPORATE SOURCE: Tech. Hochschule, Braunschwweig, Germany
SOURCE: Naturwissenschaften (1962), 49, 325-6
CODEN: NATWAY; ISSN: 0028-1042
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
GI For diagram(s), see printed CA Issue.
AB The Hofmann degradation of tetrahydroisoquinolyl phenyl carbinols (I) [Angew Chemical 74, 184(1962)] showed the degradation to a vinyl base occurred but that it was accompanied by a hydrolytic cleavage of the C-1 to C-9 bond. The question of whether hydrolysis occurred before or after the Hofmann degradation was investigated. For exptl. proof of this question, DL-4,4-dimethyl-9-hydroxylaudanosine-MeI (II) was synthesized from vanillin as follows (R = OMe throughout this abstract): 3,4-R2C6H3CMe2CH2NH2 (III) [Knabe and Kubitz, CA 56, 8688e] and 3,4-R2C6H3CH2COCl gave 3,4-R2C6H3CMe2-NHOCCH2C6H3R2-3,4, m. 168°, which was treated with POCl3 in C6H6 to give IV; IV was treated immediately with iodine and KOAc in EtOH to give V, double m.p. 74° and 126°, the lower-melting form being convertible to the higher-melting form; reduction of V with NaBH4 gave VI, oil, λ 282 mμ, broad bands at 3280 cm.-1, giving a pos. reaction for aminoethanol with Cu++/OH-; VI treated with MeI in presence of base gave II, m. 232° (decomposition). In II both H atoms are in the β-position to the N atom of the pyridine ring so that no Hofmann degradation to vinyl base can occur. Under the conditions of the Hofmann degradation were formed from II 3,4-R2C6H3CHO (as well as 3,4-R2C6H3-CO2H by a Cannizzaro reaction) and VII, m. 247° (decomposition), whose constitution was proved by synthesis from the N-formyl derivative of III. This result showed that the C-1 to C-9 bond was cleaved before the actual Hofmann degradation of I. If hydrolysis had occurred after Hofmann degradation then II should have been unchanged.

Searcher : Shears 571-272-2528

IT **95133-88-3**, Ketone, 3,4-dihydro-6,7-dimethoxy-4,4-dimethyl-1-isoquinolyl 3,4-dimethoxyphenyl
(preparation of)
RN 95133-88-3 CAPLUS
CN Ketone, 3,4-dihydro-6,7-dimethoxy-4,4-dimethyl-1-isoquinolyl 3,4-dimethoxyphenyl (7CI) (CA INDEX NAME)



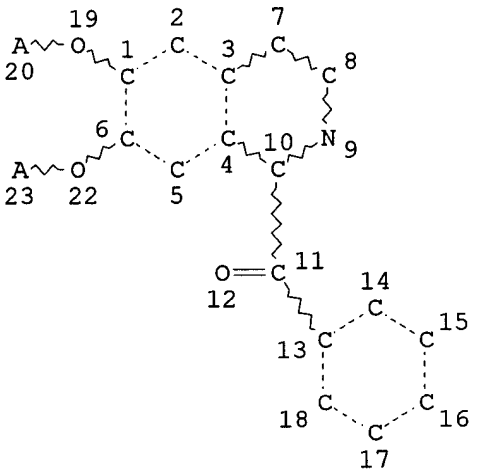
FILE 'CAOLD' ENTERED AT 12:36:36 ON 28 OCT 2004
L12 2 S L10

L12 ANSWER 1 OF 2 CAOLD COPYRIGHT 2004 ACS on STN
AN CA61:6988f CAOLD
TI synthesis of 1-(4-methoxybenzoyl)-N-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline
AU Wiegrebe, Wolfgang
IT 1484-85-1 1485-00-3 1653-64-1 17606-20-1 17606-35-8 20341-14-4 20341-46-2 20345-69-1 20345-83-9 **95133-88-3**

L12 ANSWER 2 OF 2 CAOLD COPYRIGHT 2004 ACS on STN
AN CA57:11251c CAOLD
TI synthesis and hydrolytic degradation of DL-4, 4-dimethyl-9-hydroxylaudanosine methiodide
AU Wiegrebe, Wolfgang; Awe, W.
IT **95133-88-3** 95138-37-7 95941-21-2 96002-06-1 97767-60-7 101295-83-4

FILE 'USPATFULL' ENTERED AT 12:36:57 ON 28 OCT 2004
L13 0 S L10

(FILE 'MARPAT' ENTERED AT 12:37:11 ON 28 OCT 2004)
L14 STR



NODE ATTRIBUTES:
NSPEC IS RC AT 20
NSPEC IS RC AT 23
CONNECT IS M3 RC AT 7
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L16 4 SEA FILE=MARPAT SSS FUL L14 (MODIFIED ATTRIBUTES)
L17 3 SEA FILE=MARPAT ABB=ON PLU=ON L16/COMPLETE

L17 ANSWER 1 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 140:375087 MARPAT
TITLE: Preparation of bicyclic benzamides as histamine H3 receptor ligands useful in the treatment of neurological diseases
INVENTOR(S): Best, Desmond John; Orlek, Barry Sidney
PATENT ASSIGNEE(S): Glaxo Group Limited, UK
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004037788	A1	20040506	WO 2003-EP11650	20031020

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: GB 2002-24557 20021022
GB 2003-6328 20030319

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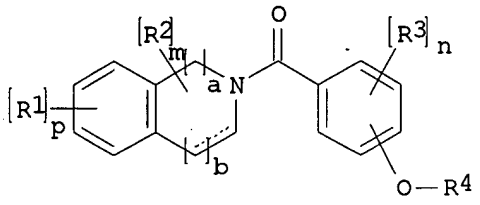

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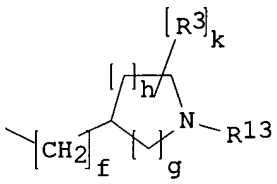
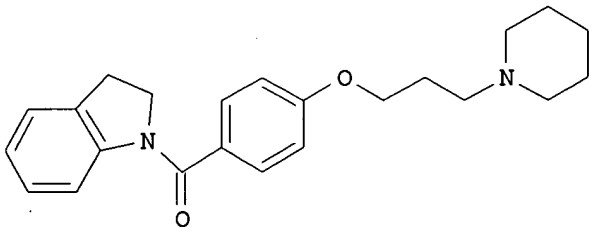


II



III

AB The title compds. [I; R1, R2 = halo, OH, CN, etc.; a, b = 0-2 (a and b cannot both = 0); R3 = halo, alkyl, alkoxy, CN, NH2, CF3; m, n = 0-2; p = 0-3 (when p = > 1 then two R1 may instead be linked to form a heterocyclyl); R4 = (CH2)qNR11R12, II (wherein q = 2-4; R11, R12 = alkyl; or NR11R12 = (un)substituted heterocyclyl; R13 = H, alkyl, cycloalkyl, alkylaryl, heterocyclyl; R14 = halo, alkyl, haloalkyl, OH, dialkylamino, alkoxy; f, k = 0-2; g = 0-2 and h = 0-3 (g and h cannot both be 0))], useful in the treatment of neurol. and psychiatric disorders, were prepared Thus, reacting 4-[3-(piperidin-1-yl)propoxy]benzoic acid hydrochloride (preparation given) with indoline afforded III which exhibited pKb ≥ 8.5 in the histamine H3 functional antagonist assay. The pharmaceutical composition comprising the compound I is claimed.

IC ICM C07D209-26
ICS C07D217-06; C07D209-44; C07D209-32; C07D215-08; C07D403-04; C07D223-16; C07D409-04; C07D491-04; C07D403-12; A61K031-4035; A61K031-404; A61K031-47; A61K031-55; A61P025-00
CC 27-21 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
ST bicyclic benzamide prepn histamine H3 receptor antagonist neurol disease; indole indoline isoindoline benzazepine benzoyl prepn histamine H3

antagonist
IT Histamine receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(H3; preparation of bicyclic benzamides as histamine H3 receptor ligands useful in the treatment of neurol. diseases)
IT Human
Mental disorder
Nervous system, disease
Nervous system agents
(preparation of bicyclic benzamides as histamine H3 receptor ligands useful
in the treatment of neurol. diseases)
IT 685564-54-9P 685564-55-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of bicyclic benzamides as histamine H3 receptor ligands useful
in the treatment of neurol. diseases)
IT 685564-45-8P 685564-46-9P 685564-47-0P 685564-48-1P 685564-49-2P
685564-50-5P 685564-51-6P 685564-52-7P 685564-53-8P 685564-56-1P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclic benzamides as histamine H3 receptor ligands useful
in the treatment of neurol. diseases)
IT 67-64-1, Acetone, reactions 87-86-5, Pentachlorophenol 91-21-4,
1,2,3,4-Tetrahydroisoquinoline 100-46-9, Benzylamine, reactions
104-58-5, 3-(Piperidin-1-yl)propan-1-ol 108-30-5, Succinic anhydride,
reactions 109-70-6, 1-Bromo-3-chloropropane 110-89-4, Piperidine,
reactions 120-47-8, Ethyl 4-hydroxybenzoate 120-72-9, Indole,
reactions 123-75-1, Pyrrolidine, reactions 443-82-3 496-12-8,
Isoindoline 496-15-1, Indoline 927-58-2, 4-Bromobutanoyl chloride
1191-95-3, Cyclobutanone 1194-02-1, 4-Fluorobenzonitrile 4424-20-8,
2,3,4,5-Tetrahydro-1H-3-benzazepine 22190-33-6, 5-Bromoindoline
32372-82-0, Isoindoline hydrochloride 38404-42-1 46053-72-9
55831-04-4, 1,2-Bis(bromomethyl)-4-fluorobenzene 57584-71-1,
5-Fluoroisoindoline 60702-69-4, 2-Chloro-4-fluorobenzonitrile
109384-19-2, N-(tert-Butoxycarbonyl)-4-piperidinol 123018-23-5,

7-Methanesulfonyl-2,3,4,5-tetrahydro-1H-3-benzazepine 149355-52-2, 7-Cyano-1,2,3,4-tetrahydroisoquinoline 171084-93-8, 6-Cyano-1,2,3,4-tetrahydroisoquinoline hydrochloride 194853-86-6, 4-Fluoro-2-trifluoromethylbenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of bicyclic benzamides as histamine H3 receptor ligands useful
in the treatment of neurol. diseases)

IT 75912-94-6P, Ethyl 4-(3-chloropropoxy)benzoate 127168-94-9P, N-Benzyl-5-(methoxycarbonyl)isoindoline 149353-71-9P, N-(tert-Butoxycarbonyl)-5-(carboxy)isoindoline 263888-56-8P, N-(tert-Butoxycarbonyl)-5-cyanoisoindoline 333954-86-2P, 4-[(1-(tert-Butoxycarbonyl)-4-piperidinyl)oxy]benzonitrile 368441-44-5P, N-(tert-Butoxycarbonyl)-5-(methoxycarbonyl)isoindoline 397275-27-3P, 4-[(1-(Cyclobutyl)-4-piperidinyl)oxy]benzonitrile 583880-66-4P, 2-Chloro-4-[(1-(tert-butoxycarbonyl)-4-piperidinyl)oxy]benzonitrile 685565-08-6P, Ethyl 4-(3-(piperidin-1-yl)propoxy)benzoate 685565-09-7P, 4-(3-(Piperidin-1-yl)propoxy)benzoic acid hydrochloride 685565-10-0P, 4-(3-(Piperidin-1-yl)propoxy)benzoyl chloride hydrochloride 685565-11-1P, 4-(3-(Piperidin-1-yl)propoxy)-2-trifluoromethylbenzonitrile 685565-12-2P, 4-(3-(Piperidin-1-yl)propoxy)-2-trifluoromethylbenzoic acid 685565-13-3P, 4-(3-(Piperidin-1-yl)propoxy)-2-trifluoromethylbenzoyl chloride 685565-14-4P, N-Benzyl-5-fluoroisoindoline 685565-15-5P, 5-Fluoroisoindoline hydrochloride 685565-16-6P, N-Benzyl-4-fluoroisoindoline 685565-17-7P, Pentachlorophenyl 4-(3-(piperidin-1-yl)propoxy)benzoate 685565-18-8P, N-(tert-Butoxycarbonyl)-5-(aminocarbonyl)isoindoline 685565-19-9P, 5-Cyanoisoindoline trifluoroacetate 685565-20-2P, N-(tert-Butoxycarbonyl)-5-[(pyrrolidin-1-yl)carbonyl]isoindoline 685565-22-4P, 5-[(Pyrrolidin-1-yl)carbonyl]isoindoline hydrochloride 685565-23-5P, N-(tert-Butoxycarbonyl)-5-[(morpholin-4-yl)carbonyl]isoindoline 685565-25-7P, 5-[(Morpholin-4-yl)carbonyl]isoindoline trifluoroacetate 685565-26-8P, 4-(4-Piperidinyloxy)benzonitrile trifluoroacetate 685565-27-9P, 4-[(1-(Cyclobutyl)-4-piperidinyl)oxy]benzoic acid hydrochloride 685565-28-0P, 4-[(1-(Cyclobutyl)-4-piperidinyl)oxy]benzoyl chloride hydrochloride 685565-29-1P, 2-Chloro-4-(3-(piperidin-1-yl)propoxy)benzonitrile 685565-30-4P, 2-Chloro-4-(3-(piperidin-1-yl)propoxy)benzoic acid hydrochloride 685565-31-5P, 2-Chloro-4-(3-(piperidin-1-yl)propoxy)benzoyl chloride hydrochloride 685565-32-6P, 2-Chloro-4-(4-piperidinyloxy)benzoic acid hydrochloride 685565-33-7P, 2-Chloro-4-[(1-isopropyl-4-piperidinyl)oxy]benzonitrile 685565-34-8P, 2-Chloro-4-[(1-isopropyl-4-piperidinyl)oxy]benzoic acid hydrochloride 685565-35-9P, 2-Chloro-4-[(1-isopropyl-4-piperidinyl)oxy]benzoyl chloride hydrochloride 685565-36-0P, 2-Chloro-4-[(1-cyclobutyl-4-piperidinyl)oxy]benzonitrile 685565-37-1P, 2-Chloro-4-[(1-cyclobutyl-4-piperidinyl)oxy]benzoic acid hydrochloride 685565-38-2P, 2-Chloro-4-[(1-cyclobutyl-4-piperidinyl)oxy]benzoyl chloride hydrochloride
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclic benzamides as histamine H3 receptor ligands useful
in the treatment of neurol. diseases)

L17 ANSWER 2 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 119:249691 MARPAT
TITLE: Novel substituted salicyclic acids

INVENTOR(S): Agback, Karl Hubert; Ahrgren, Leif; Berglindh, Thomas; Haraldsson, Martin; Olsson, Lars Inge; Smedegaard, Goeran
PATENT ASSIGNEE(S): Kabi Pharmacia AB, Swed.
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9310094	A1	19930527	WO 1992-SE758	19921104
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9229589	A1	19930615	AU 1992-29589	19921104
AU 668528	B2	19960509		
EP 613468	A1	19940907	EP 1992-924067	19921104
EP 613468	B1	20000712		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 07501330	T2	19950209	JP 1993-509191	19921104
JP 3259915	B2	20020225		
HU 69723	A2	19950928	HU 1994-1391	19921104
HU 221476	B	20021028		
RU 2124501	C1	19990110	RU 1994-28109	19921104
AT 194597	E	20000715	AT 1992-924067	19921104
CZ 287285	B6	20001011	CZ 1994-1207	19921104
ES 2149780	T3	20001116	ES 1992-924067	19921104
SK 282080	B6	20011008	SK 1994-547	19921104
CA 2123697	C	20031209	CA 1992-2123697	19921104
IL 103665	A1	19970814	IL 1992-103665	19921106
US 5302718	A	19940412	US 1992-973753	19921109
LV 10246	B	19950420	LV 1992-202	19921113
ZA 9208864	A	19930513	ZA 1992-8864	19921117
LT 3182	B	19950327	LT 1992-229	19921117
CN 1088918	A	19940706	CN 1993-100015	19930102
CN 1042631	B	19990324		
US 5403930	A	19950404	US 1993-132874	19931007
NO 9401799	A	19940622	NO 1994-1799	19940513
FI 9402289	A	19940517	FI 1994-2289	19940517
US 5556855	A	19960917	US 1994-365869	19941229
GR 3034585	T3	20010131	GR 2000-402274	20001009
PRIORITY APPLN. INFO.:			SE 1991-3397	19911118
			CS 1994-1207	19921104
			WO 1992-SE758	19921104
			US 1992-973753	19921109
			US 1993-132874	19931007

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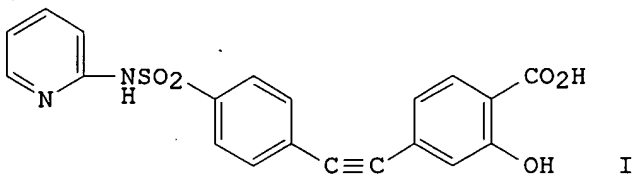

I

AB The title compds. Het-NRSO2Ph1APh2(CO2H)(OH) (Het = heterocyclic ring; Ph1, Ph2 = benzene ring wherein the carboxylate and hydroxy group are in ortho position to each other; A = bridge which is stable against reduction since it is not azo), salts and derivs. thereof are claimed. The use of these compds. for the treatment of autoimmune diseases is claimed. The compds. thus claimed are analogs of sulfasalazine. Thus, 2-hydroxy-5-[[4-[(2-pyridylamino)sulfonyl]phenyl]ethynyl]benzoic acid (I) was prepared in several steps. A 250μM concentration of I inhibited concacavaliln A-induced lymphocyte proliferation by 95.6%, whereas sulfasalazine inhibited by 53.7%. I also inhibited superoxide production in human ganulocytes.

IC ICM C07D213-75
ICS C07D261-16; C07D239-42; C07D237-20; C07D277-82

CC 25-17 (Benzene, Its Derivatives, and Condensed Benzenoid Compounds)
Section cross-reference(s): 1, 27

ST immunomodulator salicylate deriv prepn; immune modulator salicylate deriv prepn; pyridylaminosulfonylethynyl salicylate deriv prepn

IT Immunostimulants
([[(aminosulfonyl)phenyl]alkyl]salicylates)

IT Autoimmune disease
(treatment of, [[(aminosulfonyl)phenyl]alkyl]salicylate for)

IT 149556-48-9P 149556-49-0P 149556-50-3P 149556-51-4P 149556-52-5P
149556-53-6P 149556-54-7P 149556-55-8P 149556-56-9P 149556-57-0P
149556-58-1P 149556-59-2P 149556-60-5P 149556-61-6P 149556-62-7P
149556-63-8P 149556-64-9P 149556-65-0P 149556-66-1P 149556-67-2P
149556-68-3P 150320-57-3P 150320-58-4P 150320-59-5P 150320-60-8P
150320-61-9P 150320-62-0P 150320-63-1P 150343-86-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as immunomodulator)

IT 345-29-9P 1737-21-9P 15125-87-8P 15206-70-9P 60977-44-8P
61393-01-9P 119754-18-6P 119754-22-2P 148901-14-8P 149532-91-2P
149532-92-3P 149532-93-4P 149532-94-5P 149532-95-6P 149556-69-4P
149556-70-7P 149556-71-8P 149556-72-9P 149556-73-0P 149556-74-1P
149556-75-2P 149556-76-3P 149556-79-6P 149556-80-9P 149556-81-0P
149556-82-1P 149556-83-2P 149556-84-3P 149556-86-5P 149556-87-6P
149556-88-7P 149556-89-8P 149556-90-1P 149556-91-2P 149556-92-3P
149556-93-4P 149556-94-5P 149556-95-6P 149556-96-7P 151164-21-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as intermediate for [[(aminosulfonyl)phenyl]alkyl]salicylate (immunomodulator))

IT 98-61-3, 4-Iodobenzenesulfonyl chloride 115-19-5 119-30-2, 2-Hydroxy-5-iodobenzoic acid 1072-67-9 1603-40-3, 3-Methyl-2-pyridinamine 4068-75-1, Methyl 2-hydroxy-5-iodobenzoate 13110-96-8 50702-38-0 64062-91-5, 4-(2-Bromoethyl)benzenesulfonyl chloride 149556-77-4 149556-78-5 149556-85-4

RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for [[(aminosulfonyl)phenyl]alkyl]salicylate (immunomodulator))

L17 ANSWER 3 OF 3 MARPAT COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 118:22153 MARPAT
TITLE: Preparation of (4-quinolylmethyl)benzoates and analogs as drugs
INVENTOR(S): Clemence, Francois; Fortin, Michel; Haesslein, Jean Luc
PATENT ASSIGNEE(S): Roussel-UCLAF, Fr.
SOURCE: Eur. Pat. Appl., 88 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 498722	A1	19920812	EP 1992-400295	19920205
EP 498722	B1	19970730		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
FR 2672595	A1	19920814	FR 1991-1373	19910207
FR 2672595	B1	19950519		
FR 2680509	A1	19930226	FR 1991-10434	19910820
FR 2680509	B1	19950728		
JP 04338378	A2	19921125	JP 1992-47749	19920205
JP 3531944	B2	20040531		
AT 156120	E	19970815	AT 1992-400295	19920205
ES 2104862	T3	19971016	ES 1992-400295	19920205
CA 2060771	AA	19920808	CA 1992-2060771	19920206
US 5324839	A	19940628	US 1992-832003	19920206
US 5478938	A	19951226	US 1994-216035	19940322
PRIORITY APPLN. INFO.:			FR 1991-1373	19910207
			FR 1991-10434	19910820
			US 1992-832003	19920206

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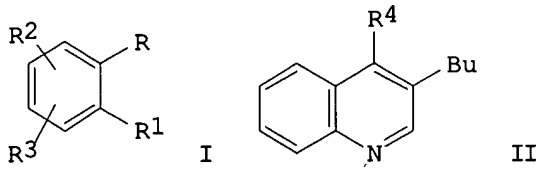

AB Title compds. [I; RR1 = Z1:Z2:Z3:Z4 wherein, e.g., 1 of Z1-Z4 = N, 1 of the remaining Z = (substituted)-CCH2Ph, and the others = N or (substituted)methine; R2,R3 = H, halo, alkyl, aryl, CONH2, etc.] were prepared as cardiovascular agents, psychoanaleptics, etc. (no data). Thus, BuCH2CO2Et was condensed with (CO2Et)2 and the product condensed with PhNH2 to give PhNHC(CO2Et):CBuCO2Et which was cyclized and the product converted in 2 steps to quinoline II (R4=Cl). The latter was condensed

with 4-(BrH2C)C6H4CN to give, after hydrolysis, II [R4 = CH2C6H4(CO2H)-4].

IC ICM C07D215-12
ICS A61K031-395; C07D215-14; C07D215-233; C07D237-32; C07D239-88; C07D241-38; C07D237-28; C07D215-36

CC 27-17 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

ST quinolylmethylbenzoate prepn drug; cardiovascular quinolylmethylbenzoate prepn; gastrointestinal qunolylmethylbenzoate prepn

IT Cardiovascular agents
((quinolylmethyl)benzoates and analogs)

IT Disease
(gynecol. treatment of, quinolylmethyl)benzoates and analogs for)

IT Digestive tract
(disease, treatment of, (quinolylmethyl)benzoates and analogs for)

IT Kidney, disease
(failure, treatment of, quinolylmethyl)benzoates and analogs for)

IT Artery, disease
(stenosis, post-angioplasty, treatment of, (quinolylmethyl)benzoates and analogs for)

IT 2417-72-3P, Methyl-4-bromomethylbenzoate 25870-62-6P, 1-Phenyl-2-hexanone 76469-88-0P, Methyl-4-cyanomethylbenzoate 87378-94-7P 116491-50-0P 135015-64-4P 144624-23-7P 144624-24-8P 144624-25-9P 144624-26-0P 144624-27-1P 144624-28-2P 144624-29-3P 144624-30-6P 144624-31-7P 144624-32-8P 144979-38-4P 144979-55-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in preparation of drugs)

IT 144624-12-4P 144624-13-5P 144624-14-6P 144624-15-7P 144624-16-8P 144624-17-9P 144624-18-0P 144624-19-1P 144624-20-4P 144624-21-5P 144624-22-6P 144979-40-8P 144979-41-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as drug)

IT 62-53-3, Aniline, reactions 95-92-1, Diethyloxalate 103-80-0, Phenylacetylchloride 123-66-0, Ethylcaproate 591-78-6, 2-Hexanone 615-43-0 693-02-7, 1-Hexyne 1461-25-2, Tetrabutyl tin 6232-88-8, 4-Bromomethylbenzoic acid 7737-62-4 17201-43-3, 4-Bromomethylbenzonitrile
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of drugs)

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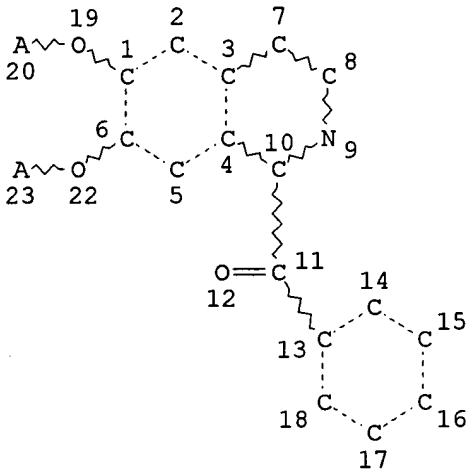

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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 22

STEREO ATTRIBUTES: NONE

ATTRIBUTES SPECIFIED AT SEARCH-TIME:
ECLEVEL IS LIM ON ALL NODES
ALL RING(S) ARE ISOLATED

L18 0 SEA FILE=MARPATPREV SSS FUL L1 (MODIFIED ATTRIBUTES)

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SEARCH TIME: 00.00.01

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L19 0 S L10

FILE 'HOME' ENTERED AT 12:42:44 ON 28 OCT 2004